

## INTERNATIONAL SEARCH REPORT

Internat Application No  
PCT/93/03966

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/705 C12N9/48 G01N33/68 G06F19/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>YU X CHRISTOPHER ET AL: "Identification of N-linked glycosylation sites in human testis angiotensin-converting enzyme and expression of an active deglycosylated form"</p> <p>JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 272, no. 6, 1997, pages 3511-3519, XP002269906</p> <p>&amp; ISSN: 0021-9258</p> <p>See Material and Methods, page 3518 and Fig. 8 and last paragraph of conclusion the whole document</p> <p style="text-align: center;">----- -/--</p>	1-41, 48-58

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

12 February 2004

Date of mailing of the international search report

25/02/2004

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

Intern al Application No  
PCT 03/03966

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WHITTLE P J ET AL: "PROTEIN STRUCTURE-BASED DRUG DESIGN" ANNUAL REVIEW OF BIOPHYSICS AND BIOMOLECULAR STRUCTURE, ANNUAL REVIEWS INC., PALO ALTO, CA, US, vol. 23, 1994, pages 349-375, XP001008225 ISSN: 1056-8700 see page 350-352, Fig. 1, page 355 and summary the whole document	1-41, 48-58
Y	----- GSCHWEND D A ET AL: "MOLECULAR DOCKING TOWARDS DRUG DISCOVERY" JOURNAL OF MOLECULAR RECOGNITION, HEYDEN & SON LTD., LONDON, GB, vol. 9, 1996, pages 175-186, XP000882526 ISSN: 0952-3499 the whole document see in particular the different possible ligand docking strategies	28-41, 48-56
A	----- WO 91/00354 A (INST NAT SANTE RECH MED) 10 January 1991 (1991-01-10) the whole document	1-41, 48-58
A	----- EP 0 444 605 A (UNITIKA LTD) 4 September 1991 (1991-09-04) the whole document	1-41, 48-58
P,X	----- DATABASE PROTEIN DATA BANK 'Online! PDB; PDB Identification code 108A 7 February 2003 (2003-02-07), NATESH R. ET AL.: "Crystal structure of human ACE (native)" XP002269910 retrieved from WWW.RCSB.ORG accession no. 108A the whole document	1-41, 48-58
P,X	----- GORDON KERRY ET AL: "Deglycosylation, processing and crystallization of human testis angiotensin-converting enzyme." BIOCHEMICAL JOURNAL, vol. 371, no. 2, 15 April 2003 (2003-04-15), pages 437-442, XP002269907 & ISSN: 0264-6021 the whole document	1-41, 48-58
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	KIM HO MIN ET AL: "Crystal structure of Drosophila angiotensin I-converting enzyme bound to captopril and lisinopril." FEBS LETTERS. 13 MAR 2003, vol. 538, no. 1-3, 13 March 2003 (2003-03-13), pages 65-70, XP002269908 ISSN: 0014-5793 the whole document	1-41, 48-58
T	NATESH RAMANATHAN ET AL: "Crystal structure of the human angiotensin-converting enzyme-lisinopril complex." NATURE (LONDON), vol. 421, no. 6922, 30 January 2003 (2003-01-30), pages 551-554, XP002269909 & ISSN: 0028-0836 the whole document	1-41, 48-58

# INTERNATIONAL SEARCH REPORT

Int. application No.  
PCT/GB 03/03966

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 46-47  
because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 42-45  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Claims Nos.: 46-47

Claims 46-47 relate to presentation of information (Rule 39.1(v) PCT) Concerning claims 46-47 applicant's attention is drawn to Rule 39.1(v) PCT. The subject-matter of claims 46-47 refers to the presentation of structure data and is not regarded as patentable invention within the meaning of Rule 67 (v) PCT since it relates to a presentation of information (protein model structure coordinates) as a coordinate listings (or structure factor data) and their use, or information stored on a computer or computer readable media. Thus, the above mentioned claims will not be searched.

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Continuation of Box I.2

Claims Nos.: 42-45

Claims 42-45 relate to reach-through compounds and their use in methods or pharmaceutical composition:

Present claims 42-44 relate to an "ACE modulator" defined by reference to a its potential action on the ACE activity.

The claims cover all products having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for no such products (only the known inhibitors are mentioned in the description). In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT).

A meaningful search cannot be established because it is not possible to determine if any of the presently known substances is falling under the terms of these "modulators" use/product claims. Besides it is noted, that the use of compounds of claim 42 are not rendered novel just because of the fact that the compounds have been identified by the method of claims 28-36, e.g. such compounds and their specific use can already exist.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5),

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

should the problems which led to the Article 17(2) declaration be overcome.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9100354	A	10-01-1991	FR 2649412 A1	11-01-1991
			AT 238423 T	15-05-2003
			CA 2035888 A1	06-01-1991
			DE 69034060 D1	28-05-2003
			DK 432254 T3	11-08-2003
			EP 0432254 A1	19-06-1991
			ES 2195992 T3	16-12-2003
			WO 9100354 A1	10-01-1991
			JP 4500612 T	06-02-1992
			US 5801040 A	01-09-1998
EP 0444605	A	04-09-1991	JP 3251543 A	11-11-1991
			DE 69103042 D1	01-09-1994
			DE 69103042 T2	22-12-1994
			EP 0444605 A2	04-09-1991
			US 5098887 A	24-03-1992
			US 5243027 A	07-09-1993